Zika FAQs for Clinicians

*This document was updated on May 17, 2016, and content will be updated as the situation changes.

How is Zika virus transmitted?

Zika virus is transmitted to humans primarily through the bite of an infected *Aedes* species mosquito—the same type of mosquito that spreads dengue, chikungunya, and yellow fever. *Aedes* mosquitoes are aggressive daytime biters and feed both indoors and outdoors. Zika virus can be transmitted from a pregnant mother to her fetus during pregnancy or around the time of birth. We do not know how often perinatal transmission of Zika virus occurs. There are case reports of possible transmission via blood transfusion or sexual contact.

An MMWR from February 26, 2016, reported 6 new cases of sexual transmission of Zika virus investigated by CDC and state public health departments. CDC continues to emphasize that the primary mode of Zika virus transmission is through the bite of an infected mosquito. People who have Zika virus infection can protect others by preventing additional mosquito bites. Based on what we know now, sexual partners can protect each other by using condoms to prevent spreading sexually transmitted infections. Zika virus has been detected in semen of symptomatic men and can persist in semen longer than blood; however, the duration of persistence in semen is unknown and it is unknown if infected men who do not develop symptoms can have Zika virus in their semen. The Zika virus has also been identified in saliva and urine, but the likelihood of transmission from these sources is unknown. Further guidance will be shared as information becomes available.

What is the epidemiology of Zika virus disease (or Zika)?

The infection rate is 73% with a symptomatic attack rate of 18%. All age groups can be affected. Disease is typically mild and does not lead to hospitalizations or deaths. Zika occurs in tropical areas with large mosquito populations, and is known to circulate in Africa, the Americas, Southern Asia and Western Pacific. Zika virus was discovered in 1947, but for many years only sporadic human cases were detected in Africa and Southern Asia. In 2007, the first documented outbreak of Zika virus disease occurred in the Pacific. Since 2013, cases and outbreaks of the disease have been reported from the Western Pacific, the Americas, and Africa.

Who is at risk of infection?

Anyone who is living in or traveling to an area where Zika virus is found who has not already been infected with Zika virus is at risk of infection. Those who do not travel to affected areas are currently at low risk of acquiring the infection via mosquitoes because local, mosquito-linked transmission has not been reported in the continental U.S. (as of this writing). Because competent mosquito vectors are located in Virginia, it is possible that local transmission of Zika virus via mosquitoes could occur during Virginia's mosquito season (May through October). For a map of where the mosquitoes that could spread Zika virus are located in the U.S., see http://www.cdc.gov/zika/vector/range.html. The risk of acquiring Zika via sexual transmission is unknown. Specific areas where Zika virus transmission is ongoing are often difficult to determine and are likely to change over time. Please visit CDC's Zika Travel Information webpage for the most updated information.

How can Zika virus infection be prevented?

There is no vaccine to prevent Zika. Natural immunity follows infection. Travelers can protect themselves by taking steps to prevent mosquito bites. Use insect repellent; wear long-sleeved shirts and long pants; and stay in places with air conditioning or with window and door screens. Pregnant women can and should choose an EPA-registered insect repellent and use it according to the product label. Women who cleared the infection prior to becoming pregnant cannot transmit Zika to their fetus.

Zika virus usually remains in the blood of an infected person for about a week, but it can be found longer in some people. Therefore, to prevent introduction and spread of Zika virus into local mosquitoes, infected persons are recommended to remain in their homes or wear protective clothing and mosquito repellent during the first week of illness.

Regarding the possibility of sexual transmission of Zika virus:

- The risk of sexual transmission of many infections is eliminated by abstaining from sexual activity and the risk can be reduced by consistent and correct use of condoms.
- Men who reside in or have traveled to an area of active Zika virus transmission who have a pregnant partner should abstain from sexual activity or consistently and correctly use condoms during sex (i.e., vaginal intercourse, anal intercourse, or fellatio) for the duration of the pregnancy. Pregnant women should discuss their male partner's potential exposures to mosquitoes and history of Zika-like illness with their healthcare provider.
- Men who reside in or have traveled to an area of active Zika virus transmission who are concerned about sexual transmission of Zika virus might consider abstaining from sexual activity or using condoms consistently and correctly during sex.

What are symptoms of Zika?

The range of incubation period of Zika is likely 3-14 days after exposure. Characteristic clinical findings are acute onset of fever with maculopapular rash, arthralgia, or conjunctivitis. Other commonly reported symptoms include myalgia and headache. Clinical illness is usually mild with symptoms lasting for several days to a week. Viremia persists up to 1 week after symptom onset. Severe disease requiring hospitalization is rare.

The illness may be mistaken for dengue virus or chikungunya virus infections; clinical features comparing Zika, Dengue, and Chikungunya are described below:

Features	**Zika**	**Dengue**	**Chikungunya**
Fever	++	+++	+++
Rash	+++	+	++
Conjunctivitis	++	-	-
Arthralgia	++	+	+++
Myalgia	+	++	+
Headache	+	++	++
Hemorrhage	-	++	-
Shock	-	+	-

For the current outbreak in the Americas, some countries, including Brazil, Columbia, El Salvador, Suriname and Venezuela, are reporting an increase in Guillain-Barré Syndrome cases and other neurologic conditions. A review of data from the Zika outbreak in French Polynesia also revealed identification of microcephaly and other neurologic syndromes, such as GBS, in a small proportion of patients.

What is the treatment for Zika?

There is currently no cure, but the symptoms of Zika can be treated with pain and fever-reducing medications like acetaminophen, rest, and plenty of fluids to prevent dehydration. Patients should not take aspirin or non-steroidal anti-inflammatory drugs until dengue virus is ruled out.

Is there any association between Zika and congenital microcephaly?

Scientists at the CDC have concluded, after careful review of existing evidence, that Zika virus is a cause of microcephaly and other severe fetal brain defects. Microcephaly describes a baby or child with a smaller than normal brain and head. Increasing evidence from a number of recently published studies and a careful evaluation using established scientific criteria supports these conclusions. It does not mean, however, that all women who have Zika virus infection during pregnancy will have babies with problems. CDC's media statement on this new conclusion can be found here. Studies are still underway to learn more about health conditions associated with Zika virus and the effects of Zika virus infection during pregnancy.

What gaps do we have in our understanding of Zika?

Key issues to be addressed in our understanding of Zika include:

- Epidemiological characteristics of the virus
- Potential medical countermeasures (including treatments and vaccines) that can be developed.
- How Zika virus interacts with other arboviruses (viruses that are transmitted by mosquitoes, ticks and other arthropods) such as dengue.
- Development of more specific laboratory diagnostic tests for Zika virus that can reduce misdiagnosis that may occur due to the presence of dengue or other viruses in a test sample.

Laboratory testing

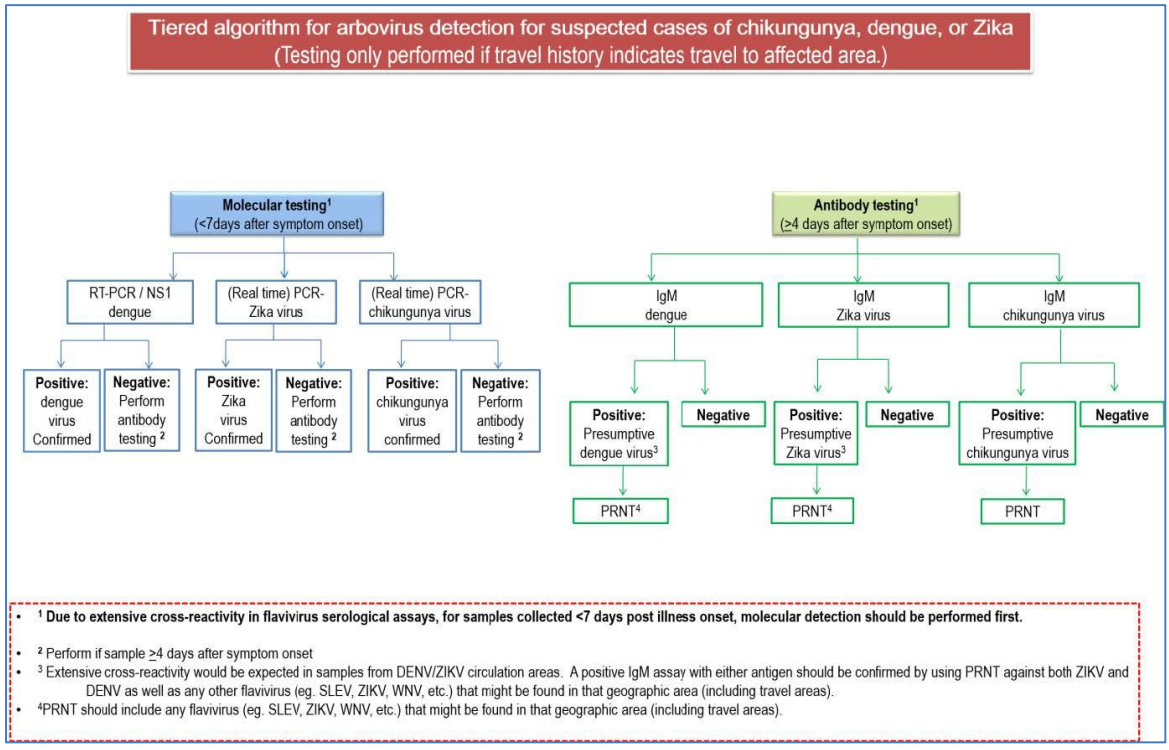
What types of testing for Zika virus are available?

Healthcare providers should contact their local health department to facilitate testing. Virginia's state laboratory, the Division of Consolidated Laboratory Services (DCLS), now has testing capacity for Zika virus through RT-PCT (serum and urine specimens) and IgM. DCLS is also assisting with specimen submission and shipping to CDC when warranted. Commercial testing is now offered through Focus Diagnostics, Inc. (RT-PCR in serum only).

There are no commercially available laboratory tests for Zika. CDC is currently the only lab that can test specimens from Virginia for Zika virus and testing at CDC includes RT-PCR and antibody testing (IgM and plaque-reduction neutralizing tests (PRNT)). Because the Zika virus is strongly sero-cross reactive with other flaviviruses (e.g., dengue virus and WNV), submission of an acute serum specimen (collected within 7 days of symptom

onset and, ideally, between 3 and 7 days after onset) for RT-PCR is encouraged. Urine specimens can be submitted (in conjunction with a serum specimen) up to 14 days after symptom onset. Immunologic testing must rely on IgM serology and the use of the virus-specific Plaque Reduction Neutralization Test (PRNT). IgM antibodies are expected to be present about 1 week after symptom onset and can persist for up to 12 weeks. The figure below from the CDC laboratory testing guidelines below shows the recommended molecular or antibody testing based on the symptom onset date.

Because of overlapping clinical presentations, testing for chikungunya, dengue and Zika should be considered. DCLS is able to test for chikungunya (RT-PCR and serology) and dengue (PCR). DCLS is expected to have Zika virus testing capability in the near future, but any testing for Zika needs to be done at the CDC until assays have been validated at DCLS. This will require that specimens be sent to DCLS for forwarding to CDC for Zika testing.



Source: CDC Division of Vector-Borne Diseases, Arboviral Diseases and Dengue Branches. Memorandum: Updated diagnostic testing for Zika, chikungunya, and dengue viruses in US Public Health Laboratories. January 13, 2016. Available at: http://www.cdc.gov/zika/pdfs/denvchikvzikv-testing-algorithm.pdf.

What are the challenges in interpreting Zika virus testing?

RT-PCR test may not demonstrate Zika virus RNA in a woman with Zika if the period of viremia has passed. Serum serologic testing can be performed; however, cross-reactivity with related flaviviruses (e.g., dengue, and yellow fever viruses) is common. Plaque-reduction neutralization testing (PRNT) can be performed to measure virus-specific neutralizing antibodies to Zika virus, but neutralizing antibodies may still yield cross-reactive results in persons who were previously infected with another flavivirus, such as dengue, or has been vaccinated against yellow fever or Japanese encephalitis. It is important to work closely with your local health department to ensure the appropriate test is ordered and interpreted correctly.

Zika and Pregnancy

What is the Zika Pregnancy Registry?
To understand more about Zika virus infection during pregnancy and congenital Zika virus infections, CDC has established the US Zika Pregnancy Registry. Data collected through this surveillance effort will help guide recommendations for clinical care and testing, plan for services for pregnant women and families affected by Zika virus, and improve prevention of Zika virus infection during pregnancy. Local health departments may reach out to health care providers caring for pregnant women who have laboratory evidence of Zika virus infection (regardless of symptoms) and their infants. As more details emerge, VDH will inform providers. Preliminary information can be found on the CDC's US Zika Pregnancy Registry website.

What is known about the effects of Zika virus on pregnant women?
We expect that the course of Zika is similar to that in the general population. No evidence exists to suggest that pregnant women are more susceptible or experience more severe disease during pregnancy. It is not known if pregnant women are more susceptible to Guillain-Barré syndrome.

Is there any association between Zika and congenital microcephaly?
Scientists at the CDC have concluded, after careful review of existing evidence, that Zika virus is a cause of microcephaly and other severe fetal brain defects. Additional studies are underway to investigate further details about timing of infection, risk of birth defects, and other relevant scientific questions.

Is there any known association between maternal Zika and other adverse pregnancy outcomes?
The full spectrum of outcomes that might be associated with Zika during pregnancy is unknown and requires further investigation.

How should pregnant patients who are considering travel to an area with Zika virus transmission be counseled?
CDC recommends that pregnant women in any trimester should consider postponing travel to an area where Zika virus transmission is ongoing. If a pregnant woman is considering travel to one of these areas, she should talk to her healthcare provider. If she travels, she should strictly follow steps to avoid mosquito bites during the trip.

Which pregnant women should be tested for Zika?
Testing should be performed in consultation with local health departments. Pregnant women that fall into any of the following categories are recommended to be tested for Zika:

A. Pregnant women who traveled to a Zika-affected area within the previous 12 weeks:
    - If symptomatic*, the preference is to collect a serum specimen within 3–7 days of symptom onset for RT-PCR; otherwise collect specimen for IgM serology and PRNT;
    - If asymptomatic, collect serum specimen 2–12 weeks after travel for IgM serology;

B. Pregnant women (with or without symptoms of Zika) who have a sexual partner† who traveled to a Zika-affected area and had symptoms of Zika during or within 2 weeks of travel or was confirmed to have Zika
C. Pregnant women who did not travel to a Zika-affected area and do not have an ill sexual partner who traveled, but who have a history of mosquito bite(s) and have ≥2 symptoms of Zika

*Symptoms of Zika are: fever, rash, arthralgia, or conjunctivitis; OR complications of pregnancy (e.g., fetal loss in 2nd or 3rd trimester, microcephaly, intracranial calcifications).
†Sexual partner refers only to individuals who had sex without using barrier protection (during vaginal intercourse, anal intercourse, or oral sex).

See VDH's testing webpage for a testing algorithm.

What are the potential sequelae of microcephaly?
For infants diagnosed with microcephaly, head size correlates with underlying brain size. However, these measurements do not consistently predict long term sequelae. Neurologic sequelae may include seizures, vision or hearing problems, and developmental disabilities. Symptoms vary with the extent of brain disruption. More information on microcephaly can be found here: http://www.cdc.gov/ncbddd/birthdefects/microcephaly.html

What causes congenital microcephaly?
Causes of congenital microcephaly may include genetic conditions such as chromosomal abnormalities or maternal exposures (e.g., alcohol, mercury, or radiation) during pregnancy. Maternal infections that have been associated with microcephaly include cytomegalovirus (CMV), herpes simplex virus, rubella virus, lymphocytic choriomeningitis virus (LCMV), *Treponema pallidum* (i.e., syphilis), and *Toxoplasma gondii.*

Information on infants with Zika

What treatment exists for infants with congenital Zika?
No treatment is currently available for Zika. Care for these infants is focused on diagnosing and managing conditions that are present, monitoring the child's development over time, and addressing problems as they arise.

What is the prognosis for a newborn with congenital Zika?
The prognosis for infants with congenital Zika is not known. In infants with severe microcephaly from other causes, a range of neurologic sequelae have been reported (e.g., intellectual disability, hearing loss, vision loss, and seizures). These problems can range from mild to severe, are often life-long, and in some cases can be life-threatening.

Which newborns should be tested for Zika?
Testing for Zika virus is recommended for infants born to women who traveled to or resided in an area with ongoing Zika virus transmission during pregnancy who were 1) diagnosed with microcephaly or intracranial

calcifications detected prenatally or at birth, or 2) who have mothers with positive or inconclusive test results for Zika.

If a mother had Zika during pregnancy, should she breastfeed her infant?

Although Zika virus RNA has been detected in breast milk, Zika infection caused by breastfeeding has not been documented. Based on available evidence, the benefits of breastfeeding infants outweigh any theoretical risk related to Zika virus transmission.

CDC's updated guidance on Zika

- Update: Interim Guidance for Prevention of Sexual Transmission of Zika Virus — United States, 2016 (March 25, 2016)
    - o Update provides recommended time intervals for taking precautions to reduce the risk of sexual transmission after travel to areas with active Zika virus transmission or after Zika virus infection.
- Update: Interim Guidance for Health Care Providers Caring for Women of Reproductive Age with Possible Zika Virus Exposure — United States, 2016 (March 25, 2016)
    - o Update includes recommendations on counseling women
- Summary of Updated Interim Zika Clinical Guidance for Reproductive Age Women and Men, Sexual Transmission of Zika, and the U.S. Zika Pregnancy Registry, from COCA call on April 12, 2016:
- All of CDC's MMWR Reports on Zika

References:

- http://www.who.int/features/qa/zika/en/
- http://www.cdc.gov/zika/hc-providers/qa-pregnant-women.html
- http://www.cdc.gov/zika/hc-providers/qa-pediatrician.html
- http://emergency.cdc.gov/coca/ppt/2016/01_26_16_zika.pdf
- http://www.bt.cdc.gov/coca/ppt/2016/04_12_16_zikaclinicalguidelines_fb.pdf
- Musso D, Roche C, Nhan TX, Robin E, Teissier A, Cao-Lormeau VM. Detection of Zika virus in saliva. J Clin Virol. 2015; 68:53-5. http://dx.doi.org/10.1016/j.jcv.2015.04.021
- Gourinat AC, O'Connor O, Calvez E, Goarant C, Dupont-Rouzeyrol M. Detection of Zika virus in urine. Emerg Infect Dis [Internet]. 2015 Jan [February 7, 2016]. http://dx.doi.org/10.3201/eid2101.140894.